

**WEST****End of Result Set**

Generate Collection

5,010,010

L2: Entry 14 of 14

File: USPT

Apr 23, 1991

US-PAT-NO: 5010010DOCUMENT-IDENTIFIER: US 5010010 A

TITLE: Production of human parathyroid hormone from microorganisms

DATE-ISSUED: April 23, 1991

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gautvik; Kaare M.	Oslo			NOX
Alestrom; Peter	Sollihogda			NOX
Oven; Tordis B.	Oslo			NOX
Gabrielsen; Odd S.	Oslo			NOX

US-CL-CURRENT: 435/252.3; 435/252.33, 435/254.21, 435/320.1, 435/69.4,  
435/69.9, 536/23.51

## CLAIMS:

We claim:

1. A DNA sequence encoding Saccharomyces mating factor alpha 1 operably linked to human parathyroid hormone wherein said DNA sequence can stably transform a yeast cell to express and secrete an intact human parathyroid hormone.
2. The DNA sequence of claim 1 wherein said DNA sequence comprises the nucleotide sequence set forth in FIG. 11.
3. The yeast cell of claim 1 wherein said cell is in the genus Saccharomyces.
4. The yeast cell of claim 1 wherein said cell is of the species Saccharomyces cerevisiae.
5. The yeast cell of claim 1 wherein said cell is a budding yeast cell.
6. The human parathyroid hormone of claim 1 wherein said hormone has biological activity substantially equivalent to naturally occurring human parathyroid hormone.
7. A plasmid comprising the DNA sequence of claim 1.
8. A plasmid according to claim 7 wherein said nucleotide sequence comprises: ##STR2##
9. A plasmid according to claim 7 wherein the nucleotide sequence comprises: ##STR3##
10. A plasmid according to claim 7 wherein the nucleotide sequence comprises: ##STR4##
11. A plasmid according to claim 7 wherein the nucleotide sequence comprises: ##STR5##
12. A microorganism containing the plasmid of claim 8.
13. A microorganism according to claim 12 wherein said microorganism is Escherichia coli.
14. A microorganism containing the plasmid of claim 9.
15. A microorganism according to claim 14 wherein the microorganism is Escherichia coli.
16. A microorganism containing the plasmid of claim 10.
17. A microorganism according to claim 16 wherein the microorganism is Escherichia coli.
18. A microorganism containing the plasmid of claim 11.

19. A microorganism according to claim 18 wherein the microorganism is *Escherichia coli*.
20. A plasmid according to claim 7, wherein the nucleotide sequence comprises: ##STR6##
21. The plasmid of claim 7, wherein the nucleotide sequence comprises: ##STR7##
22. A microorganism containing the plasmid of claim 7.
23. A transformed yeast cell comprising a DNA sequence encoding *Saccharomyces* mating factor alpha 1 operably linked to human parathyroid hormone, said cell capable of expressing said DNA and secreting said expressed DNA into an extracellular environment, whereby said secreted, expressed DNA is intact human parathyroid hormone.
24. The transformed yeast cell of claim 23 wherein said DNA sequence comprises the nucleotide sequence of FIG. 11.
25. The transformed yeast cell of claim 23 wherein said yeast cell is of the genus *Saccharomyces*.
26. The transformed yeast cell of claim 23 wherein said yeast cell is of the species *Saccharomyces cerevisiae*.
27. The transformed yeast cell of claim 23 wherein said yeast cell is a budding yeast cell.
28. The transformed cell of claim 23 wherein said expressed human parathyroid hormone has a biological activity substantially equivalent to naturally occurring human parathyroid hormone.
29. A DNA sequence comprising a vector capable of stably transforming yeast wherein said DNA sequence encodes *Saccharomyces* mating factor alpha 1 operably linked to human parathyroid hormone wherein said vector can stably transform a yeast cell to express and secrete an intact human parathyroid hormone.
30. The transformed yeast cell of claim 29 wherein said yeast cell is a budding yeast.
31. The vector of claim 30 wherein said vector is an autonomous replicating plasmid.
32. The vector of claim 30 wherein said vector is an integrating plasmid.
33. The transformed yeast of claim 30 wherein said yeast is from the genus *Saccharomyces*.
34. The transformed yeast of claim 30 wherein said yeast is of the species *Saccharomyces cerevisiae*.
35. A plasmid, pSSHPTH-10, deposited in the American Type Culture Collection under ATCC No. 40267.
36. A transformed *E. coli* containing pSSHPTH-10, deposited in the American Type Culture Collection under ATCC No. 67223.
37. A transformed *S. cerevisiae* containing pSS.alpha.L.times.5-HPTH1, deposited in the American Type Culture Collection under ATCC No. 20821.
38. A plasmid, pSS.alpha.L.times.5-HPTH1, deposited in the American Type Culture Collection under ATCC No. 40266.

**WEST****End of Result Set**☐ **Generate Collection**5,420,242

L1: Entry 2 of 2

File: USPT

May 30, 1995

US-PAT-NO: 5420242DOCUMENT-IDENTIFIER: US 5420242 A

TITLE: Production of human parathyroid hormone from microorganisms

DATE-ISSUED: May 30, 1995

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gautvik; Kaare M.	Oslo			NOX
Alestrom; Peter	Sollihogda			NOX
Oyen; Tordis B.	Oslo			NOX

US-CL-CURRENT: 530/307; 536/23.51

## CLAIMS:

We claim:

1. An isolated intact, functional human parathyroid hormone that is resistant to degradation by a KEX2 like proteolytic enzyme between the amino acids in positions 26 and 27 thereof.
2. The intact, functional human parathyroid hormone of claim 1 wherein Lys in position 26 is substituted with Gln.
3. An intact human parathyroid hormone operably linked to a modified Saccharomyces mating factor alpha 1 wherein a tetramer Glu-Ala-Glu-Ala, disposed immediately N-terminal to said human parathyroid hormone is omitted.
4. An intact human parathyroid hormone operably linked to the Lys Arg KEX2 cleavage site of the leader sequence of Saccharomyces mating factor alpha 1.
5. An intact human parathyroid hormone operably linked to the first 19 amino acids of Saccharomyces mating factor alpha 1.
6. A DNA sequence encoding Saccharomyces mating factor alpha 1 operably linked to a DNA sequence encoding human parathyroid hormone wherein said DNA sequence stably transforms a yeast cell to express and secrete an intact, functional human parathyroid hormone that is resistant to degradation by a KEX2 like proteolytic enzyme between the amino acids in positions 26 and 27 thereof.
7. The DNA sequence encoding Saccharomyces mating factor alpha 1 operably linked to a DNA sequence encoding human parathyroid hormone wherein said DNA sequence encoding human parathyroid hormone is modified such that the codon encoding Lys in position 26 thereof encodes Gln.
8. A DNA sequence encoding Saccharomyces mating factor alpha 1 operably linked to a DNA sequence encoding human parathyroid hormone wherein said DNA sequence encoding said mating factor alpha 1 is modified by deletion of the codons encoding the tetramer Glu-Ala-Glu-Ala disposed immediately N-terminal to said DNA sequence encoding human parathyroid hormone.
9. A DNA sequence encoding Saccharomyces mating factor alpha 1 and human parathyroid hormone wherein said DNA sequence encoding said human parathyroid hormone is operably linked to a DNA sequence encoding the Lys Arg KEX2 cleavage site of the leader sequence of Saccharomyces mating factor alpha 1.
10. A DNA sequence encoding the first 19 amino acids of Saccharomyces mating factor alpha 1 and human parathyroid hormone wherein the DNA sequence encoding human parathyroid hormone is operably linked to a portion of a DNA sequence

encoding the first 19 amino acids of said Saccharomyces mating factor alpha 1 and wherein said DNA sequence encoding the first 19 amino acids of Saccharomyces mating factor alpha 1 and human parathyroid hormone which stably transforms a yeast cell to express and secrete on intact, functional human parathyroid hormone.